

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)



(51) International Patent Classification ⁶ :	A1	(11) International Publication Number:	WO 96/22803
A61M 16/12, 16/10		(43) International Publication Date:	1 August 1996 (01.08.96)

(21) International Application Number:	PCT/SE96/00068	(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AZ, BY, KG, KZ, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
(22) International Filing Date:	24 January 1996 (24.01.96)	
(30) Priority Data:	9500251-5 25 January 1995 (25.01.95) SE	
(71) Applicant (for all designated States except US): LOFLO AB [SE/SE]; Norra Kyrkvägen 11, S-428 50 Källered (SE).		
(72) Inventor; and		
(75) Inventor/Applicant (for US only): STENQUIST, Ola [SE/SE]; Aschebergsgatan 41A, S-411 33 Göteborg (SE).		
(74) Agents: GRADUMS, Valdis et al.; Albihn West AB, P.O. Box 142, S-401 22 Göteborg (SE).		

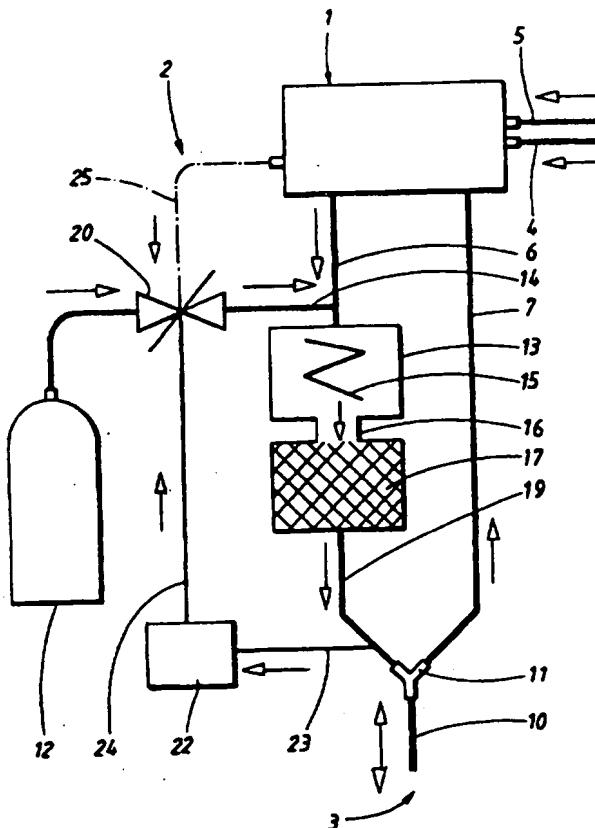
Published

With international search report.
In English translation (filed in Swedish).

(54) Title: METHOD AND APPARATUS FOR MEDICAL TREATMENT VIA RESPIRATORY ORGAN.

(57) Abstract

Method and assembly for the preparation of a gas mixture intended for medical treatment via the respiratory system by means of a treatment gas, such as nitrogen monoxide. The gas mixture is prepared by introducing the treatment gas with an uniform flow into an oxygen-containing gas, after which the compound mixture is brought through an absorber (17), arranged to absorb unwanted products from the reaction between the oxygen and the treatment gas.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

TITLE:

5

Method and apparatus for medical treatment via respiratory organ.

TECHNICAL FIELD:

10

The present invention relates to a method and an assembly for the preparation of a gas mixture for medical treatment by means of medically active compounds supplied via the respiratory system of a patient. The supply of nitrogen monoxide is thereby especially referred to.

15

PRIOR ART:

20

The oxygenation which the patient himself can bring about through his respiration is, in certain medical conditions, insufficient. In not too severe conditions, it may be sufficient to supply additional oxygen gas in the inhalation air and in other cases furthermore a compulsory pulmonary ventilation. In certain conditions, e.g. severe weakness conditions, or during the period of intensive care after a major operation, and also during cardiac or pulmonary operations, not even the use of respirator and raised oxygen level is sufficient in order to achieve a satisfactory oxygenation. A reason for this has turned out to be that a compound important for the uptake of oxygen from the pulmonary vesicles, namely nitrogen monoxide, which improves the adaptation between inhaled oxygen and the blood flow passing the lungs in order to be oxygenated, is produced by the patient to an extent which is too small. Through this discovery the solution has been reached of, in said severe conditions, improving the ventilation-circulation conditions by means of the addition of nitrogen monoxide (NO) to the inhalation air in a highly determined proportion. It has thereby been shown that a grave lack of oxygen in the blood may be corrected.

30

It is important that NO is added in a proportionally minute amount, which is accurately regulated and which is

40

determined for each separate treatment case. Assemblies have therefore been developed with a mechanical ventilator and an accurately working mixing equipment for the gases which are to be supplied to the patient: air, oxygen and 5 nitrogen monoxide in nitrogen gas.

An assembly of the described type will be very complicated and has to be provided with electronically controlled valves, which ensure that the correct amounts of said gases 10 are supplied to the patient in a correctly tuned respiratory rhythm.

In order to avoid the need to acquire such complicated and costly equipment in its entirety, when said treatment is 15 needed, attempts have been made to produce apparatuses, which are a complement to the mechanical ventilators always to be found in intensive care departments, which ventilators are arranged for an automatic, rhythmical supply of an inhalation gas to the patient. The thought behind this has been to set up a supplementary equipment 20 for the supply of the treatment gas, NO, to the gas flow emitted from the ventilator to the patient.

Such a supply apparatus is known from EP, A1, 0 589 751. To 25 this is connected a supply conduit for the treatment gas to the outlet from a ventilator, where said outlet is connected to a patient system consisting of a supply tube, the inhalator portion, and an outlet tube, the expiration portion, connected together next to the patient with an Y-coupling.

The normal respiratory gas is supplied to the patient in an even rhythm, meaning that the flow in the inhalator portion 35 is at its maximum during inhalation and zero during expiration. In order to be able to obtain an uniform concentration of the supplied NO-gas, the NO-supply must be

synchronized with the ventilation by means of a valve controlling the supply, making it occur only during active inhalation, which leads to a uniform concentration of NO in the gas inhaled by the patient. In order to achieve this,
5 the supply conduit is provided with a valve, which is arranged to open when an over-pressure in a special conduit from the ventilator indicates that gas for inhalation is supplied. In this way, the gas supply is brought to occur rhythmically during the inhalation moments.

10

Such an arrangement will be relatively complicated, partly because the rhythmically working dosing equipment in itself will be complicated, and partly because the two systems, ventilator and dosing apparatus, have to be connected
15 together and adjusted to produce a supply of a mixture with the correct proportions.

20

In order to simplify the system it has, in other connections, been proposed to supply the treatment gas in the inhalator portion of the patient system after the ventilator in an accurately controlled, continuous flow. However, when treating with NO, this causes the gas inhaled by the patient to obtain a varying concentration because
25 the continuous NO-flow has arrived in the inhalator portion of the respiratory system during inhalation with a high gas flow, leading to a low NO-concentration, and during expiration when the gas stands still in the respiratory system and may cause extremely high peaks of the NO-concentration in the gas subsequently inhaled by the patient. The non-uniform mixture leads to NO of a high concentration coming into close contact with oxygen gas of a high concentration, which leads to the formation of nitrogen dioxide, which is extremely poisonous and the amount of which must be minimized. A non-uniform mixture
30 also causes the lungs to receive different concentration of
35

the treatment gas in different parts, which might cause a deteriorated treatment result.

SUMMARY OF THE INVENTION:

5 The above-mentioned possibility of simplification, to supply the treatment gas in a continuous uniform flow, is utilized in the assembly according to the invention. According to the invention, the above-mentioned disadvantage of non-uniform NO-concentration in the inhaled
10 gas and subsequent formation of NO₂ is, however, avoided by supplying the NO-gas continuously to a mixing chamber in the inhalator portion of the respiratory system and thereafter allowing it to pass through a chamber with a material which especially absorbs NO₂.

15 Thus, one obtains a simple apparatus, but avoids the quality of the gas flow becoming difficult to control. In order to increase the accuracy of the dosage beyond what is possible by controlling the continuous gas flow, one can ensure that the resulting NO-content does not exceed a chosen limit by analysing the inhalation gas and arranging for influence on the dosage flow of NO to be controlled by the measured value for NO and/or NO₂.
20

25 DESCRIPTION OF THE DRAWINGS:

The enclosed drawing is shows an embodiment of the invention in a block diagram.

PREFERRED EMBODIMENT:

30 A block diagram of the assembly according to the invention is shown in the drawing. The assembly may be said to comprise three main components: a ventilator 1, a device 2 for supply of the treatment gas and for proportioning of the same, and a patient system 3. The ventilator 1 is arranged to rhythmically supply breathing gas to the patient system 2 and through this on to the patient in
35

order to maintain the breathing of the same. Such ventilators with control and checking devices are well known from the technique of intensive care and anaesthesia and need not to be closer described herein. However, it
5 should be mentioned that there is a supply conduit 4 for oxygen, O₂, to the ventilator 1, and a supply conduit 5 for air. A conduit 6 leads from the ventilator for the supply of breathing gas, accordingly a tuned mixture of the gases from the supply conduits 4 and 5, to the patient, and a conduit 7 for the reception of gas from the patient. The
10 gas which is supplied to the patient system from the conduit 6 is, as understood, designed for the inhalation of the patient and the conduit 7 is designed for receiving gas from the expiration of the patient. In the conduits or the
15 ventilator there are valves, which ensure that the gas flow only occurs in the specified direction. This direction of flow is shown with arrows in the drawing. Further, it is shown in the drawing that the ventilator may be provided with an additional connection 8. From this a measurement
20 test result, specifying the volume of breathing gas received by the patient, can be emitted in the form of an electric signal or a gas pressure. Such connections for said measurement signal exist on most ventilators.

25 The design of the patient system is also well-known but yet it is shown in the drawing, that a collection conduit 19, via a Y-coupling 11, is connected to the conduits 6 and 7 from the ventilator 1. The collection conduit 10 in turn is connected to the respiratory organs of the patient,
30 preferably through a tube inserted into the windpipe of the patient.

The connection between the patient system 3 and the ventilator 1 for the expiration gas, consequently the conduit 7, may, as shown in the drawing, be made directly without any other instruments than said valves. The
35

connection between the patient system and the conduit 6 is on the other hand made via the device for supply of the treatment gas.

5 The device 2 for supply of the treatment gas consists of the following main parts: a source for supply of the treatment gas. A gas bottle 12 is shown here and since it is presumed here that the treatment gas is nitrogen monoxide, NO, in nitrogen gas, the gas bottle is
10 accordingly filled with this gas under pressure. Further, there is included a mixing chamber 13, to which is connected a conduit 14, connected to the gas bottle 12 and to the conduit 6 for the reception of inhalation gas from the ventilator 1. Some type of flow-affecting member 15 for
15 the intimate mixing of the breathing gas from the ventilator and the treatment gas from the gas source may be inserted in the mixing chamber 13. Further, the mixing chamber 13 has an outlet 16 to an absorption chamber 17. The absorption chamber contains a compound which absorbs
20 nitrogen dioxide, NO₂, but on the whole not NO, O₂ or N₂. Such a compound may be soda-lime, the use of which is known from the technique of anaesthesia. From the mixing chamber 17 the gas purified from NO₂ may be emitted to the Y-coupling 11 of the patient system via a conduit 19.
25

As mentioned it is very important that NO is proportioned very accurately in proportion to the breathing gas from the ventilator and thereby in a minute proportion. This is achieved by controlling the supply to the mixing chamber 13, via the conduit 14, very accurately. For this purpose a control valve 20 is arranged in the conduit 14 between the gas source 12 and the mixing chamber 13.

30 One form of control by means of the control valve 20 is to measure the proportion of NO directly before the patient system 3. This can be done by supplying gas samples to a
35

gas analyzer 22, said gas samples being drawn off via a conduit 23 from the gas supply conduit for the inhalation gas with the treatment gas added, after the absorption chamber 17 and preferably as close as possible to the patient connection.

The gas analyzer 22 may be adjusted to a set point, adapted to the treatment case in question, for the proportion of treatment gas in the inhalation gas. The gas analyzer is thereby set up to emit a preferably electrical signal, via a wire 24, to the thereby electrically controlled control valve 20. The system is thereby adapted to, when the set point is exceeded, give a signal to the control valve, which causes the amount of NO supplied from the gas source to decrease, and vice versa if the set point is not reached.

A simplification may be achieved if the analyzer is only arranged for controlling a reduction of the treatment gas flow when a certain set point for NO and/or NO_2 is exceeded.

Gas analyzers of this type, adapted for the emission of a control signal when the set point for the content of a certain gas in a gas mixture is deviated from, are earlier known and several types are found on the market.

As an alternative or complement to regulating by means of a gas analyzer, the previously mentioned signal connection 8 of the ventilator may be used. This is indicated with the dot-lined wire 25 from the output 8 to the control valve 20. Since the signal from the output 8 indicates the amount of breathing gas supplied to the patient, the amount of supplied treatment gas may be determined, on the basis of the desired proportion. If the signal from the output 8 shall be used as the only means of regulation, it is still

necessary to arrange a gas analyzer for determining that a correct starting point for the proportioning is obtained. The flow through the valve is thereby tuned to the amount of breathing gas supplied during the measurement. If this
5 amount thereafter fluctuates, these fluctuations, expressed as a fluctuating signal from the output 8, may be used for such a regulation of the valve 20 that the set proportion is maintained.

10 It is also possible to realize the control system for regulation in two steps, so that, in a first step, a coarse regulation is done by means of the signal from the output 8, and a fine regulation is done by the signal from the gas analyzer.

15 By supplying the treatment gas, in accordance with the invention, in a continuous flow, when mixing with the breathing gas, a simplified equipment is obtained compared to batch-wise addition, especially concerning the devices
20 for regulation of the gas proportions. Further, a very satisfactory mixing of the entering gases is made possible, so that the supply of the treatment gas to the patient occurs uniformly all the time. Moreover, the content of NO₂ may be kept at a very low level. In systems of this type,
25 for treatment with NO, there namely occurs a reaction in the contact between NO and O₂, so that NO is oxidized to NO₂. This gas is poisonous and one should as far as possible avoid supplying it to the patient. At the same time this oxidation reduces the remaining content of NO,
30 something which is negative for the treatment result. This reaction cannot be avoided completely in any system where NO and O₂ are mixed, but the closer to the respiratory system of the patient the mixing occurs, or rather the more accurately the proportions of the different compounds can
35 be controlled, the better is the obtained treatment result.

According to the invention, the mentioned advantages from an operational point of view are achieved by, after the mixing of the breathing gas and the treatment gas, bringing this mixture through an absorber for the removal of
5 unsuitable and harmful reaction products before it is supplied to the patient. As mentioned, it is presumed herein that the treatment gas is NO, but it should not be excluded that also other treatment gases may give harmful reaction products, which may be removed by an absorber
10 adapted for this purpose.

5 CLAIMS:

1. Method for preparing a gas mixture intended for medical treatment via the respiratory system of a patient, by means of active compounds added to the gas, in the form of a treatment gas, such as especially nitrogen monoxide, whereby the gas mixture is prepared for the supply to the patient which occurs in a rhythmically varying pressure course, characterized in that the gas mixture is prepared by intermixing the treatment gas into a gas containing oxygen, which treatment gas has the inclination to form reaction products undesirable for supply to the patient, in a uniform flow and well distributed in said gas, after which the compound mixture is brought through an absorber (17) arranged to absorb said reaction products for the final preparation of the gas mixture before the supply to the patient.

2. Method according to claim 1, characterized in that the gas mixture, after having left the absorber (17) by means of a gas analyzer (22), is analyzed regarding its content of treatment gas, during determination of a set point for its proportion, whereby the analyzer is arranged to emit a control signal to a control valve (20), for regulation of the flow of treatment gas to the absorber together with the other components of the gas mixture, in such a way that when the set point is exceeded, the gas flow is reduced by means of the control valve and is preferably increased, when the set point is not reached.

3. Method according to claim 1, characterized in that the amount per unit of time of prepared gas mixture for supply to the patient is measured during the course of the treatment and that

variations in the gas amount are allowed to influence a control valve for the supply of the treatment gas during preparation of the gas mixture, in such a way that the amount of the treatment gas admixed by means of the valve
5 is increased when increased preparation and supply of the breathing gas mixture is measured, while the amount of the treatment gas is reduced on reduced supply of the breathing gas mixture.

10 4. Method according to claims 2 and 3,
characterized in that the regulation of the amount of supplied treatment gas, by means of the gas analyzer (22), is used as fine regulation and is preceded by a coarse regulation by means of measurement of the
15 amount of the supplied breathing gas mixture.

5. Assembly for carrying out the method according to any one of claims 1-4 and comprising a ventilator (1), arranged for supply of a breathing gas mixture containing oxygen to a patient via a breathing system (3), whereby an outlet (6) is arranged for supply of said gas in a rhythmically fluctuating pressure course to a patient system (3) arranged for connection to a patient, for the inhalation of the patient, and an inlet (7) which
20 is connected to the patient system (2) for reception of the expiration gas of the patient, and is provided with a device (2) for supply of treatment gas, preferably nitrogen monoxide, during preparation of the breathing gas mixture
25 characterized in that the device for supply of the treatment gas exhibits a mixing chamber (13) to which both the said outlet (6) from the ventilator (1), and a conduit (14) from a source (12) of the treatment gas, are connected, that the mixing chamber (13) has an outlet (16) to an absorber (17), which is arranged to absorb products
30 from reaction between treatment gas and compounds in the breathing gas, for instance with nitrogen monoxide as a
35

treatment gas, nitrogen dioxide through the reaction with oxygen in the breathing gas, and that the absorber with an outlet (19) is connected with a short flow-path to the patient system (3).

5

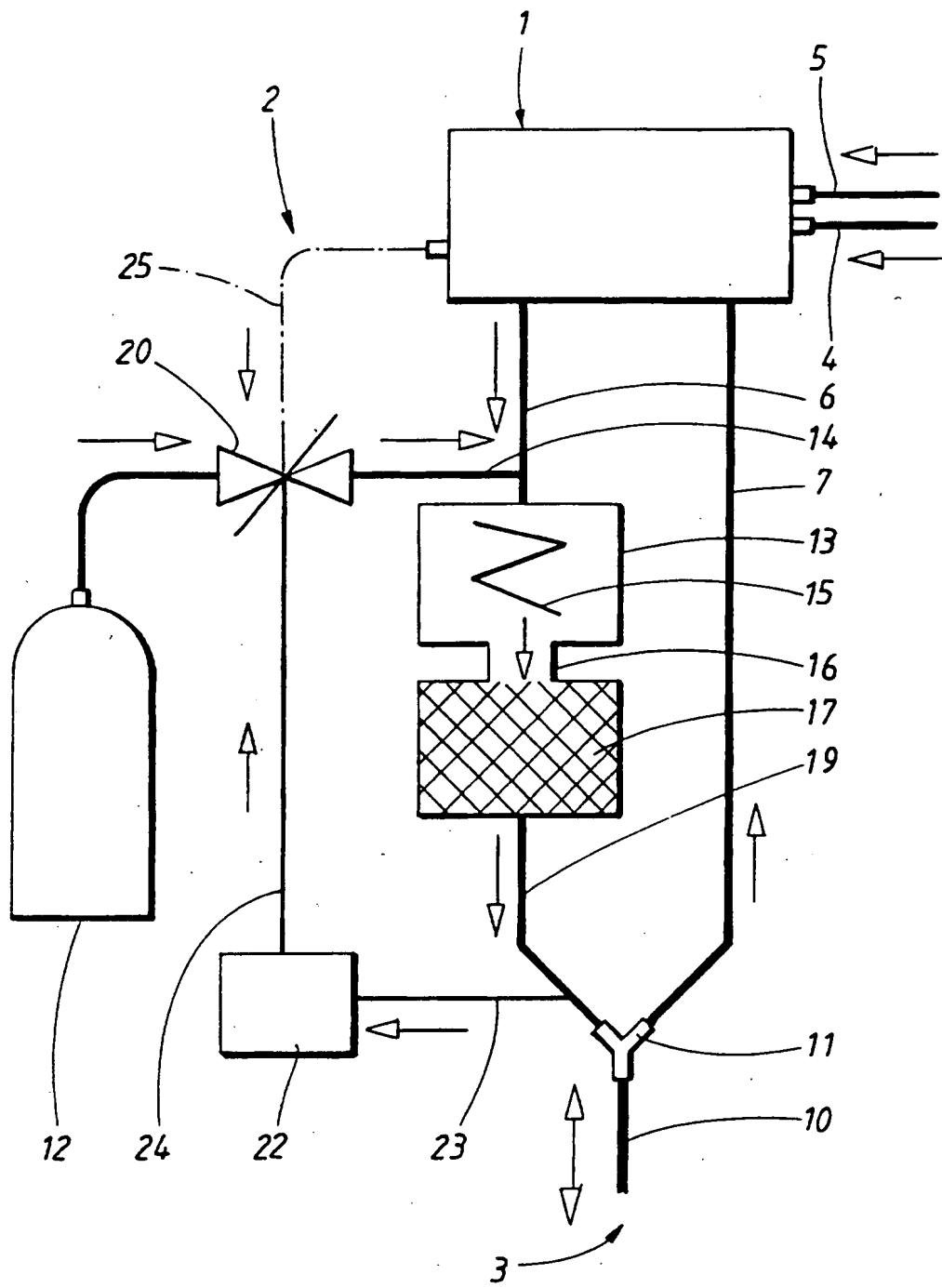
6. Assembly according to claim 5, characterized in that, a control valve (20) is arranged for the regulation of supply of the treatment gas to the treatment chamber in a principally uniform flow.

10

7. Assembly according to claim 6, characterized in that for the control of the control valve (20) a gas analyzer (22) is arranged, which is adapted to be supplied with gas samples from the outlet (19) from the absorber (17) next to the patient system (3) and adapted for the setting of a set point for the content of treatment gas in the gas mixture brought to the patient system, and arranged to emit a control signal to the control valve (20) for reducing the gas flow by means of the control valve when the set point is exceeded and increasing the flow when the set point is not reached.

8. Assembly according to claim 6, characterized in that the ventilator (1) is provided with an output (8) for a control signal, the value of which is proportionally dependent on the amount, per unit of time, of breathing gas supplied to the patient system (3), and that the control valve (20) is arranged to, by influencing said control signal, increase the amount of supplied breathing gas when an increased amount of breathing gas emitted from the ventilator (1) is indicated, and to reduce the flow of treatment gas when a reduced amount of breathing gas is indicated.

1/1



INTERNATIONAL SEARCH REPORT

International application No. PCT/SE 96/00068
--

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61M 16/12, A61M 16/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0589751 A1 (L'AIR LIQUIDE, SOCIETE ANONYME POUR L'ETUDE ET L'EXPLOITATION DES PROCEDES GEORGES CLAUDE), 30 March 1994 (30.03.94), abstract, figure --	1-8
A,P	EP 0659445 A1 (OHMEDA INC.), 28 June 1995 (28.06.95), figure 1, abstract --	1-8
A,P	EP 0640357 A1 (SIEMENS ELEMA AB), 1 March 1995 (01.03.95), figure -- -----	1-8

Further documents are listed in the continuation of Box C.

See patent family annex.

- * Special categories of cited documents
- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

07 -05- 1996

23 April 1996

Name and mailing address of the ISA/
Swedish Patent Office
Box 5055, S-102 42 STOCKHOLM
Facsimile No. + 46 8 666 02 86

Authorized officer

Håkan Sandh
Telephone No. + 46 8 782 25 00

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/SE 96/00068

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A1- 0589751	30/03/94	NONE	
EP-A1- 0659445	28/06/95	NONE	
EP-A1- 0640357	01/03/95	NONE	